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(19)

(54) ANTI INFLAMMATORY TOPICAL COMPOSITIONS

(71) We, UNILEVER LIMITED, a company organised under the laws of Great Britain, of Unilever House, Blackfriars, London E/C 4, England, do hereby declare the invention for which we pray that a patent may be granted to us and the method by which it is to be performed, to be particularly described in and by the following statement:—

The present invention relates to cosmetic compositions, more specifically to compositions for the protection and treatment of the skin.

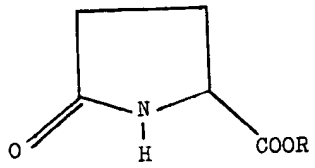
Atmospheric conditions in winter, repeated contact with detergent solutions when washing crockery and carrying out domestic chores, the sun's rays, contact with various chemical products can result in dryness of the skin, blotchiness and even in more severe damage. The current practice to obtain temporary protection is to apply an insulating layer of grease to the stratum corneum. The resultant protection is poor, short-lasting and devoid of any curative effect.

The aim of the present invention is to provide compositions for external use that can prevent or treat cutaneous irritation caused by external factors.

These compositions are characterized by the fact they contain esters of terpene alcohols with 2-pyrrolidone-5-carboxylic acid, which are physiologically active substances capable of passing through the stratum corneum into the living layers of the epidermis. In particular, these substances have a stabilizing effect on the capillary walls, an anti-inflammatory effect, and a regulating effect on the secretion of sebum.

In French Patent Specification No. 2,122,495, esters of 2-pyrrolidone-5-carboxylic acid and saturated alcohols with an alkyl chain, in particular hexadecyl 2-pyrrolidone-5-carboxylate, are suggested as active ingredients for cosmetic compositions. However, although these compounds are physiologically active, they are difficult to use in cosmetic preparations because they are insoluble in water and in oils. The esters of terpene alcohols with 2-pyrrolidone-5-carboxylic acid in the compositions according to the present invention do not have this disadvantage since they are adequately soluble in water and in oils.

The terpene esters for use in the compositions of the present invention can be represented by the general formula:



where R is a terpene alcohol selected from the following substances: menthol, borneol, geraniol and citronellol. The preferred substance for the cosmetic products is menthyl 2-pyrrolidone-5-carboxylate.

Esters with this general formula can be used with a suitable carrier by incorporating them, if desired in combination with other active substances such as vitamins, anti-inflammatory, keratolytic or disinfectant substances, in the usual preparations suitable for application to the skin, such as ointments, creams, aerosols, powders, gels, pastes, essences or lotions. The concentrations should be between 0.1 and 20%, preferably between 0.2 and 5% by weight.

Therefore the compositions according to the invention can be applied advantageously in products for the care and treatment of the skin, for preventing irritation of the skin, e.g. due to epilation with the aid of hot wax, for soothing the hyperkeratosis after shaving, acne rosacea and stings of insects. Preferably methyl 2-pyrrolidone-5-carboxylate is used in these products in concentrations between 1 and 5% by weight. The use of these compositions can also give a sensation of freshness.

The compositions according to the present invention are obtained by classical methods of organic chemistry, either by direct esterification of 2-pyrrolidone-5-carboxylic acid with the terpene alcohol in the presence of suitable catalysts and solvents, or by transesterification between the terpene alcohol and methyl 2-pyrrolidone-5-carboxylate.

2-Pyrrolidone-5-carboxylic acid can be prepared, for example, by heating glutamic acid to 180°C, as described in J. Am. Chem. Soc., 1942, page 1021. The methyl ester can be prepared by intervening in the synthesis by the classical methods.

The examples of the preparation of the compositions according to the invention and the compounds used therein are given below by way of illustration.

Preparation of menthyl 2-pyrrolidone-5-carboxylate

A mixture of 64.5 g of L-2-pyrrolidone-5-carboxylic acid (obtained as described in J. Am. Chem. Soc. 1942, page 1021), 120 g of natural L-menthol, 700 ml of benzene and 6.4 g of p-toluene sulphonic acid was boiled for 40 hours. The solution was then washed with water and sodium carbonate and concentrated. The excess menthol was removed with steam and the residue was distilled under reduced pressure. This gave 94 g of L-menthyl L-2-pyrrolidone-5-carboxylate in the form of a highly viscous yellow oily liquid.

$B.p._{0.025} = 174—180°C$ $\alpha_D = -65°$ (c = 20% ethanol)
Yield: 70%
Analysis for $C_{15}H_{25}O_3N$ (M.wt. = 267.373)

	C	H	N
Calculated %	67.38	9.42	5.24
Found %	67.55	9.68	4.90

DL-2-Pyrrolidone-5-carboxylic acid can also be used for the reaction; this gave a mixture of the DL and LL diastereoisomers which was crystallized and found to have a melting point of 67—68°C; $\alpha_D = -60$ (20% ethanol).

Finally, the same method of preparation can be used with liquid menthol, which is a mixture of stereoisomers. This gives a mixture of the stereoisomers of the ester.

Preparation of bornyl 2-pyrrolidone-5-carboxylate

A mixture of 78 g (0.6 mole) of DL-2-pyrrolidone-5-carboxylic acid, 61.7 g (0.4 mole) of borneol, 6 g of p-toluene sulphonic acid and 300 ml of toluene was refluxed for 10 hours. The solution was then washed with water and sodium bicarbonate and concentrated.

Vacuum distillation, followed by recrystallization from hexane, gave 40 g of the ester in the form of a white solid with a melting point of 78°C.

Yield: 38%
$B.p._{0.4} = 210—216°C$
Analysis for $C_{15}H_{23}O_3N$ (M.wt. = 265.357)

	C	H	N
Calculated %	67.89	8.73	5.27
Found %	67.90	9.04	5.40

Preparation of geranyl 2-pyrrolidone-5-carboxylate

Esterification was carried out as hereinbefore described, using 39 g (0.3 mole) of DL-2-pyrrolidone-5-carboxylic acid, 30.8 g (0.2 mole) of geraniol, 3 g of p-toluene sulphonic acid and 150 ml of toluene. 13 g of the ester were obtained as an oily liquid.

Yield: 25%
$B.p._{0.015} = 178—180°C$
Analysis for $C_{15}H_{21}O_3N$ (M.wt. = 263.341)

	C	H	N
Calculated %	68.41	8.03	5.31
Found %	69.01	8.94	4.99

Preparation of citronellyl 2-pyrrolidone-5-carboxylate

Esterification was carried out as hereinbefore described, by heating a mixture of 23.2 g (0.18 mole) of DL-2-pyrrolidone-5-carboxylic acid, 42.2 g (0.27 mole) of citronellol, 2.3 g of p-toluene sulphonic acid and 200 ml of toluene. 18.8 g of the ester were obtained as an oily liquid.

Yield: 38%
$B.p._{0.05} = 208°C$
Analysis for $C_{15}H_{25}O_3N$

	C	H	N
Calculated %	67.38	9.42	5.24
Found %	67.22	9.75	4.97

Solubility

The following data show the solubility of the esters in water, propylene glycol and groundnut oil, the solubility of hexadecyl 2-pyrrolidone-5-carboxylate being included for purposes of comparison.

TABLE 1

Solubility, g per 100 ml of solvent

	H_2O	Groundnut oil	Prop. glycol	Ethanol
Menthyl 2-pyrrolidone-5-carboxylate (p.c.)	0.7	5	>20	>50
Bornyl p.c.	0.05	⩽3	>10	>10
Geranyl p.c.	0.05	>10	>10	>10
Citronellyl p.c.	0.05	>5	⩽1	>50
Hexadecyl p.c.	0	0	0	5

Penetration into the skin

Penetration into the living layers of the skin was demonstrated with tritiated menthyl 2-pyrrolidone-5-carboxylate, added in the proportion of 1% to a gel (pH 7) with the following composition:

^3H Menthyl pyrrolidone carboxylate	1 %
Carboxylvinyl polymers (Carbopol) (CARBOPOL is a trade mark)	1 %
Diisopropylamine	0.8%
Propylene glycol	48.6%
Water	48.6%

The method used was that described by R. T. Tregear, Physical functions of skin, Academic Press, pp. 3 and 35.

A sample of human skin was perfused with Ringer's solution. The gel containing tritiated menthyl pyrrolidone carboxylate was applied to the surface of the epidermis. After 24 hours the depth of penetration was assessed by the " stripping ", method which consists in determining the quantity of menthyl 2-pyrrolidone-5-carboxylate present in skin samples obtained by stripping off successive layers of corneal cells with the aid of adhesive tape.

Most of the menthyl 2-pyrrolidone-5-carboxylate remained in the stratum corneum, approximately 60% of the quantity applied being found there (approximately 200 μ g per cm² of skin surface).

The living layers of the skin contained approximately 2% of the quantity applied, namely 6.5 μ g per cm².

The diffusion of menthyl 2-pyrrolidone-5-carboxylate in a 1% solution was thus investigated. In a 65:35 mixture of propylene glycol and water the passage 50% of the product into isopropyl myristate in 24 hours was observed. This method of measuring the diffusion into the skin of compounds from various vehicles is described by B. J. Poulsen in J. Pharm. Sci., 1968, *57*, 128. It was found that penetration of the esters depends on the stereochemistry of the molecule. L-menthyl D-pyrrolidone-5-carboxylate penetrates into the horny layer (17) in smaller quantities than the mixture of diastereoisomers.

The properties of the new products according to the invention were investigated by the following methods.

Determination of the effect on the permeability of the capillaries

The effect of the compounds on capillary permeability was demonstrated by the use of Evans blue (J. R. Parrat, J. Physiol., *140*, 105 (1958)).

One of the local signs of an inflammatory reaction is, inter alia, an increase in the permeability of the walls of the capillary blood vessels. This phenomenon can be demonstrated by the passage through the capillary wall of a dye injected intravenously. Substances that affect the permeability and fragility of the capillaries are assessed by this method.

It may be assumed that a substance that prevents or reduces the increase in capillary permeability brought about by local irritation will cause the inflammatory process to recede. Such a type of product would have applications in the fields of cosmetology or oral hygiene for the purpose of preventing or treating mild local benign inflammation.

Method used: Albino rabbits weighing 3—4 kg were restrained on their backs and shaved from the sternum to the pubis over a width of 8 cm. 2 ml of a 1% solution of Evans blue in physiological saline were injected into the marginal vein of the ear. After a few seconds, a standard cotton wool swab, soaked in chloroform and freed from the excess, was applied to the shaved skin for 30 seconds. The time taken for a definite blue colour to appear at the site of irritation was noted. At least four tests were carried out at different sites on each rabbit in order to determine the mean reaction time to the irritant. The product under investigation was then injected intravenously. After 15 min. irritation was provoked with chloroform, and the time of appearance of the colour was noted. Two tests were carried out on each animal. The intensity of the blue colour increased as a function of time.

The time of development of this colour is modified by products that act on the capillaries. A colour/time curve was plotted for a range of dilutions of a solution of Evans blue.

The products tested were dissolved in propylene glycol, then at the time of injection diluted in the ratio of 1:3 with a 9% solution of NaCl. The quantity injected was 7—8 mg per kg of body weight for all the products tested:

— 10% solution of menthyl 2-pyrrolidone-5-carboxylate in propylene glycol
— 10% solution of geranyl 2-pyrrolidone-5-carboxylate in propylene glycol
— 10% solution of bornyl 2-pyrrolidone-5-carboxylate in propylene glycol
— 10% solution of citronellyl 2-pyrrolidone-5-carboxylate in propylene glycol.

The mean times observed for the beginning (t_1) and end (t_2) of the colour reaction before and after the treatment were as follows:

TABLE 2

Mean time in min.	t_1	t_2	% delay of t_1	% delay of t_2
Before treatment	3.5	5.5		
After treatment with:				
geranyl 2-pyrrolidone-5-carboxylate	8.1	16.3	57	66
bornyl 2-pyrrolidone-5-carboxylate	7.8	14.2	55	61
citronellyl 2-pyrrolidone-5-carboxylate	3.6	6.5	0	15
menthyl 2-pyrrolidone-5-carboxylate	9.3	30.0	61	82

It can be seen from the above Table that the terpene esters according to the invention produce a marked delay in the appearance of the colour, more pronounced at time t_2, which indicates that these compounds reduce capillary permeability.

It was not possible to test hexadecyl 2-pyrrolidone-5-carboxylate because it is insoluble in propylene glycol, and ethyl alcohol is not suitable for this method.

It therefore appears that the application to the skin of the compounds according to the present invention strengthens the capillary walls. These products can be used in the care of the gums and the treatment of the skin, for example blotchiness.

Topical anti-erythematous activity

One of the most remarkable properties of living cells is their ability to adapt the permeability of the cell membrane in response to various stimuli. This property can be investigated very easily with the aid of an electric current, and numerous investigations have shown the non-linearity of the membranes, in other words the sudden change in resistance that occurs above a critical current intensity.

Experiments have shown that the membranes of living cells no longer exhibit the normal non-linear behaviour after exposure to ultraviolet radiation (M. Cambrai, J. Soc. Cosmet. Chem., 1973, *24*, 3—14).

It was found by the phoreographic method based on this phenomenon, described by J. Kryspin (J. Inv. Dermat. 1965, *44*, 227), that the terpene esters according to the invention enable the normal membrane response to be retained after irradiation.

Three-month old Wistar rats were irradiated with a dose of 17.4 joules per cm^2. The quantities necessary per cm^2 to preserve the normal membrane response after topical application were as follows: 2 mg of menthyl pyrrolidone carboxylate, 2.5 mg of geranyl pyrrolidone carboxylate, 3 mg of bornyl pyrrolidone carboxylate, 3 mg of citronellyl pyrrolidone carboxylate and 4 mg of pyrrolidone carboxylic acid.

Hence the compositions according to the invention enable the skin to return to its normal state after UV irradiation. This property indicates that they would be very valuable for use in sun and after-sun products.

In another series of experiments, menthyl 2-pyrrolidone-5-carboxylate, menthol, 2-pyrrolidone-5-carboxylic acid and hexadecyl 2-pyrrolidone-5-carboxylate were compared.

Irritation was provoked with croton oil, to which the product under investigation had been added.

Menthyl 2-pyrrolidone-5-carboxylate prevents the disappearance of the phoreographic response in a concentration of 0.03 M, while the other compounds are inactive in this concentration.

Another method to assess topically the anti-erythematous properties of the compositions according to the present invention consists in measuring the erythema caused

by UV radiation. The cutaneous flow of blood indeed increases significantly with the UV dose. As a result of this the measuring of the microcirculation can be used to quantify the erythema provoked by exposure of the skin to UV rays and to assess the effect of some anti-inflammatory agents on the erythematous zones. The measuring of the microcirculation of the cutaneous blood velocity can be effected by the clearance method of xenon 133 by Sejrsen (J. Appl. Physiol. *24*, 211, 1968 and Circ. Research *25*, 215, 1969).

The technique of measuring the microcirculation consists in marking the skin by gaseous diffusion of xenon 133 and following the variation of the local concentration of the radioactive indicator according to the time.

According to this method the action of two creams was compared, viz a placebo cream (Special Day Cream) with the same cream containing 3% menthyl 2-pyrrolidone-5-carboxylate (PCM).

The creams had the following composition:

Ingredient	Special Day Cream	
	Placebo %	PCM %
Anionic based on C_{16}–C_{18} saturated fatty alcohols (Lanette N, Henkel)	9.0	9.0
Cetyl palmitate (Cutina CP, Henkel)	4.0	4.0
Menthyl 2-pyrrolidone-5-carboxylate	0.0	3.0
Isopropyl isostearate	6.0	6.0
C_8–C_{12} Triglyceride (Miglyol 812, Dynamit Nobel)	9.0	9.0
Propyl P-hydroxybenzoate (Para–P)	0.1	0.1
Methyl P-hydroxybenzoate (Para–M)	0.4	0.4
1.3-Butyleneglycol	3.0	3.0
Parsol MCX (Ecran–UV, Givaudan)	1.0	1.0
Perfume	0.3	0.3
Sterilized deionized water to	100.0	100.0

The back of six anaesthetized albino Guinea-pigs was epilated with the aid of wax at least 72 hours before each treatment. The back of the animal was divided into 3 zones: a blank zone, a placebo cream zone and a PCM cream zone. The surface of the skin exposed was 5 cm^2. A treatment was allotted to each zone.

The erythema is provoked by 12 minutes' irradiation. The dose of energy received were 26 joules cm^2. The irradiations were carried out with a xenon lamp (Osram). (OSRAM is a trade mark) The UV rays with a wave-length below 290 mm, as well as the IR rays were removed by suitable filters.

The energy was measured with the aid of a thermopile.

Three successive applications of the cream were effected every 30¹ after the beginning of the irradiation by massage of the skin for one minute. Half an hour before the determination of the flow of blood, the site treated was washed with tepid water and cleaned. The microcirculation was measured 4 hours after the irradiation, the redness having reached its maximum intensity.

The resulting values of the flows of blood are expressed in ml. min.$^{-1}$. 100 g^{-1} in Table III.

TABLE 3

Guinea pig nr.	Blank f	U.V. + Placebo f	U.V. + PCM f
95	5.92	18.66	12.13
96	7.58	11.55	9.33
97	6.22	14.27	8.66
100	11.55	16.17	12.77
101	12.77	22.05	16.73
107	9.33	10.32	13.68
108	11.03	16.17	11.55
109	11.83	24.26	15.16
Total	76.23	133.45	100.01
Average	9.53	16.68	12.50

The decrease of the flow of blood f from 16.58 to 12.52 clearly shows the anti-inflammatory effect of the PCM.

The Student Fisher test (Lison L., Statistique appliquée à la biologie expérimentale — Gauthier-Villars, Paris 1968) shows that the results are significant at 95%.

Anti-inflammatory properties

The anti-inflammatory properties of menthyl 2-pyrrolidone-5-carboxylate were demonstrated in the carraghenin oedema test in rat food, which is a classical pharmacodynamic test.

The injection of carraghenin into the posterior foot of a rat produces oedema; an attempt is made to reduce the degree of oedema by administering preventive anti-inflammatory treatment. The rats were divided into two groups, one was used as a control group and the other received a solution of the test product in oil of vaseline per os one hour after the subcutaneous injection of a solution of carreghenin, which was given to both groups. The oedema was assessed by comparing the volume of the posterior feet four hours after this injection.

The results were as follows:

TABLE 4

	Menthyl 2-pyrrolidone-5-carboxylate				Hydrocortisone (control)
Dose, mg per kg	120	240	480	960	10
% reduction	18.85	20.49	15.57	15.57	42.04
Significance	S	S	S	S	S

Hydrocortisone was used for positive control to check the rats' reaction.

Menthyl pyrrolidone carboxylate is active in rats in concentrations of 120 mg per kg and above.

Demonstration of the anti-seborrhoeic effect of menthyl 2-pyrrolidone-5-carboxylate

The method described by Schaefer (J. Soc. Cosmetic Chemists, *24*, 331—352, 1973) was used for this purpose; it consists in measuring the increase in light transmitted by a matt surface after it has been applied to the skin. The difference between the percentage transmission before and after application to the skin is taken as a measure of the quantity of sebum removed.

Two cubes were applied 8 times in succession to each half of the forehead, and a measurement was taken after each application. This procedure was carried out twice a day with an interval of 5 hours.

At the end of the first and the second day one half of the forehead was treated with an alcoholic 10% solution of menthyl 2-pyrrolidone-5-carboxylate and the other half was treated with pure alcohol.

The differences in transmission were added together for the treated and for the untreated side respectively. The results obtained for 10 people are given below:

TABLE 5

No. of test participant	Untreated	Treated
1	5049.5	4343.0
2	2586.5	2319.5
3	1652.5	1415.5
4	2098.0	2090.0
5	2120.5	2070.0
6	1507.5	1586.0
7	5641.0	4987.0
8	3701.5	3655.0
9	1789.5	1674.0
10	1527.5	1299.5
Total	27674	25439.5
Average	2767.4	2543.95

$$\text{Reduction: } \frac{2767.4 - 2543.95}{27.67.4} \times 100 = 8.07\%$$

TABLE 6

Variance analysis

Source of fluctuations	Degrees of freedom	Mean squares	F
Individuals	9	39625	252
Zones	1	19041	12.1
Treatment	1	24942	15.9*
Error	8	15671	

* $p < 0.01$

Two applications of an alcoholic 10% solution of menthyl 2-pyrrolidone-5-carboxylate produced a significant reduction of 8% in the quantity of lipids on the skin by comparison with the control area treated with alcohol alone.

This procedure could not be followed with hexadecyl pyrrolidone carboxylate since this substance is not sufficiently soluble to give a 10% solution in alcohol.

The following examples illustrate the preparation of some products for the treatment and care of the skin; the composition of these preparations can, of course, be varied within the usual limits known to the expert.

Example I.

ANTI-IRRITANT LOTION

	wt.%
Bornyl 2-pyrrolidone-5-carboxylate	2
Esters of fatty acids and ethoxylated fatty alcohols	1.5
Synthetic cetyl alcohol	1.5
Ethylhexyl palmitate	0.1
Propyl p-hydroxybenzoate	0.3
Heteropolysaccharides	0.5
1,3-Butylene glycol	3
Sterile deionized water	89.3
Perfume	0.3
4% rye yellow 100 colourant	0.3

The mixture of bornyl 2-pyrrolidone-5-carboxylate, the esters of fatty acids and ethoxylated fatty alcohols, synthetic cetyl alcohol, ethylhexyl palmitate and propyl p-hydroxybenzoate was heated to melting point (approx. 70°C).

The heteropolysaccharides were dispersed in the mixture of butylene glycol and water at approx. 70°C, with stirring.

Emulsification was then carried out by pouring the mixture of fat into the aqueous solution, again with stirring.

The emulsion was cooled to 40—50°C and the perfume was dispersed in it, with stirring.

Viscosity at 25°C: 45 cp.

Example II.

ANTI-IRRITANT GEL

	wt.%
Citronellyl 2-pyrrolidone-5-carboxylate	2
Oleyl alcohol 10 EO	2
Polypropylene glycol 400	10
Carboxyvinyl polymers	0.4
Triethanolamine	0.4
Perfume	0.2
Distilled water	to 100

The citronellyl 2-pyrrolidone-5-carboxylate was dissolved in the oleyl alcohol 10 E.O., with stirring (phase A). The water was stirred and the carboxyvinyl polymers were dispersed in it at room temperature; the propylene glycol was then added and the mixture was neutralized to pH 6—7 with triethanolamine (phase 3).

Phase B was heated to 60°C, and phase A was added. The mixture was cooled, and the perfume added at 40—50°C.

Viscosity at 25°C: 375 cp.

Example III.

EMOLLIENT FOAM BATH

	wt.%
Menthyl 2-pyrrolidone-5-carboxylate	4
Polypropylene glycol	10
Sorbitan monolaurate	4
Sodium lauryl ether sulphate (28% A.D.)	78
Perfume	2
Distilled water	to 100

The menthyl 2-pyrrolidone-5-carboxylate was dissolved in the mixture of polypropylene glycol and sorbitan monolaurate by heating to 40—50°C, with stirring (phase A).

The sodium lauryl ether sulphate was dissolved in the water at 40—50°C, and the perfume was added, again with stirring (phase B). Phase B was then added into phase A, and the pH adjusted to 6.5—7 with triethanolamine. The mixture was then cooled.

Viscosity at 25°C: 150 cp.

Example IV.

EMOLLIENT CREAM

	wt.%
Geranyl 2-pyrrolidone-5-carboxylate	5
Esters of fatty acids with ethoxylated fatty alcohols	5
Ethoxylated lanolin	12
Esters of branched fatty acids from duck feather fat	3
Propyl p-hydroxybenzoate	0.1
Methyl p-hydroxybenzoate	0.2
1,3-Butylene glycol	3
Sterile deionized water	71.5
Perfume	0.2

The geranyl 2-pyrrolidone-5-carboxylate, the esters of fatty acids with ethoxylated fatty alcohols, the ethoxylated lanolin, the esters of branched fatty acids from duck feather fat and the propyl and methyl p-hydroxybenzoate were mixed and heated to melting point at 70°C with stirring (phase A).

The water was heated to 70°C, with the addition of the glycol (phase B). The perfume was added at 40—50°C.

Viscosity at 25°C: 600 cp.

Example V.

SUN CREAM

	wt.%
Menthyl 2-pyrrolidone-5-carboxylate	3.0
Anionic based on C_{16}—C_{18} saturated fatty alcohol (Lanette N, Henkel)	9.0
Cetyl palmitate (Cutina CP, Henkel)	4.0
Isopropylisostearate	6.0
Miglyol 812, Dynamit Nobel (C_8—C_{12} Triglyceride)	9.0
Propyl P-hydroxybenzoate	0.1
Methyl P-hydroxybenzoate	0.4
1.3-Butyleneglycol	3.0
Parsol MCX (Ecran U.V., Givaudan)	5.0
Perfume	0.3
Sterile deionized water to	100

Example VI.

BEAUTY CREAM

	wt.%
Anionic based on C_{16}—C_{18} saturated fatty alcohol (Lanette N, Henkel)	9.0
Cetyl palmitate (Cutina CP, Henkel)	4.0
Isopropyl isostearate	6.0
Miglyol 812, Dynamit Nobel (C_8—C_{12} triglyceride)	9.0
Propyl P-hydroxybenzoate	0.1
Methyl P-hydroxybenzoate	0.4
1.3-Butylene glycol	3.0
Parsol MCX (Ecran UV, Givaudan)	1.0
Perfume	0.3
Sterile deionized water	67.2
	100

This cream was prepared in accordance with Example IV. It is used advantageously to soothe cutaneous irritation in case of epilation with the aid of hot wax, hair hyperkeratosis and insect stings.

Pre-epilatory use gives a painless epilation which does not leave red traces as in the case with the usual method. Post-epilatory use does not give swollenness of the follicular cavity after tearing the hair.

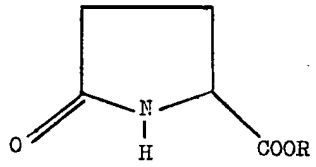
In the case of " shaver's burn ", the micro-wounds caused by the razor, a massage before and after shaving considerably relieves this smarting by soothing the irritation and causing further a slight and pleasant sensation of freshness, which reappears when the subject is warm.

In the case of acne rosacea 2 or 3 applications a day were carried out in direct contact with the epidermis. The cream can be used in larger quantities, giving a relieving effect.

The use of this cream, in the case of insect stings, gives an immediate relief to the whole swollen part and remains for an hour. Repeating the application (two, three or four times) also gives an immediate relief, but it remains 2 to 5 hours. The irritating itches have disappeared the next day.

WHAT WE CLAIM IS:—

1. Compositions for the care and treatment of the skin, characterized in that they contain at least one suitable carrier, and at least one compound having the general formula:



where R is a terpene alcohol selected from menthol, borneol, geraniol and citronellol.

2. Compositions according to claim 1, characterized in that they contain menthyl 2-pyrrolidone-5-carboxylate.

3. Compositions according to claim 1, characterized in that they contain 0.1 to 20% by weight of the compound of the general formula.

4. Compositions according to claim 1, characterized in that they contain 0.2 to 5% by weight of the compound of the said general formula.

5. Process for the preparation of the compositions according to claim 1, characterized in that a compound of the general formula is mixed with a suitable carrier.

6. Process according to claim 5, characterized in that menthyl 2-pyrrolidone-5-carboxylate is mixed with a suitable carrier.

7. Process according to claim 6, characterized in that a cream is prepared containing 0.2 to 5% by weight menthyl 2-pyrrolidone-5-carboxylate.

8. Compositions for the care and treatment of the skin according to any of claims 1 to 4 and substantially as herein described with reference to the Examples.

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